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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
STEADMAN, DAVID J

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 10/08/2002

13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/407,806	MURPHY ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 August 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,13,14 and 17-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,13,14 and 17-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Application Status

Claims 1-9, 13, 14, and 17-45 are pending in the application.

Amendment to claims 1, 5, 9, 13, 14, and 19 and addition of claims 24-45 in Paper No. 22, filed 08/13/02, is acknowledged.

Applicants' arguments presented in Paper No. 22 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Claim Objections

1. Claims 29-45 are objected in the recitation of "isolated fragment". In the interest of clarity, it is suggested that the term "nucleic acid" or "polynucleotide" be inserted before the term "fragment".

Claim Rejections - 35 USC § 112, Second Paragraph

2. Claims 1-9, 13, 14, 17-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. The rejection of claims 1 (claims 2-4, 6-9, 13, 14, and 17-23 dependent therefrom) and 5 as being indefinite in the recitation of "a polynucleotide that is complementary" is maintained. The rejection was fully explained in a previous Office action. Newly added claims 24 (claims 25-28 dependent therefrom), 32 (claims 40, 41, and 45 dependent therefrom), and 33 (claims 40, 41, and 45 dependent therefrom) are similarly indefinite in the recitation of "complement". Applicant argues (beginning at page 7 of Paper No. 22) one of skill in the art would understand the meaning of the term "complementary". Applicant argues one of skill in the art would understand the term encompasses a naturally-occurring

complementary strand with mismatches that would not be completely complementary and thus, the complementary strand need not be completely complementary. Applicants' argument is not found persuasive. The examiner disagrees with applicant's assertion that a skilled artisan would recognize that the term "complementary" encompasses polynucleotides that are non-complementary, i.e., have base mismatches. It is not the definition of the term "complementary" that is at issue. Instead, the rejection is made because a skilled artisan would not recognize the scope of complementary polynucleotides encompassed by the claims. As stated in a previous Office action, it is unclear whether applicant's claimed complementary strand is a partial (i.e., nucleic acid fragment) or a complete complement. Interestingly, applicants have defined a complement as a naturally-occurring nucleic acid with base mismatches (page 8 of Paper No. 22), a meaning that is entirely inconsistent with the art-recognized definition of "complementary". Such a definition broadens the intended scope of nucleic acids and provides further justification for the rejection. As such, a skilled artisan would not recognize the scope of complementary polynucleotides, particularly in light of applicants' own arguments. It is suggested that applicants clarify their meaning of the term "a polynucleotide that is complementary" in claims 1 and 5 with, for example, "a polynucleotide that is completely complementary". It is suggested that applicants replace "complement" with, for example, "complete complement" in claims 24, 32, and 33.

4. Claims 24 and 32 (claims 40, 41, and 45 dependent therefrom) are indefinite in the recitation of "hybridizes" as it is unclear as to the conditions used for the hybridization. The term is unclear absent a statement of the conditions under which the hybridization reaction is preformed. Nucleic acids that will hybridize under some hybridization conditions will not necessarily hybridize under different conditions. It is noted that applicants have provided "an example of oligonucleotide hybridization" conditions at page 5 of the specification. However, because the conditions are provided as an "example", it is unclear as to whether the disclosed conditions are non-limiting or other conditions are meant to be encompassed by the term. It is suggested that applicants clarify the conditions under which hybridization is to occur.

5. Claims 26 and 32 (claims 40, 41, and 45 dependent therefrom) are indefinite in the recitation of "stringent conditions" as the specification does not define what conditions constitute "stringent". What

hybridization conditions are considered "stringent" varies widely in the art depending on the individual situation as well as the person making the determination. It is noted that applicants have provided a set of conditions for hybridization at page 5 of the specification, however, it is unclear as to whether these conditions are meant to be "stringent conditions". As such, it is unclear how homologous to the sequence of a nucleic acid encoding SEQ ID NO:4, a sequence must be to be included within the scope of these claims.

6. Claims 29 (claims 35-37 and 42 dependent therefrom), 30, 31 (claims 38, 39, and 44 dependent therefrom), 33, 34, (claims 40, 41, and 45 dependent therefrom) are indefinite in the recitation of "portion of a polynucleotide". The term is not defined in the claims or the specification and it is unclear as to what part of a sequence encoding SEQ ID NO:4, the polynucleotide of claim 1, 5, or 24, or the polynucleotide of SEQ ID NO:1, 2, or 3 is meant to be included within the scope of the term "portion". For example, is the term meant to encompass only a single nucleotide or a series of nucleotides? Also, is the term meant to encompass a contiguous or non-contiguous "portion" of a nucleic acid? It is suggested that applicant clarifies the meaning of the claims.

7. Claim 29 (claims 35-37 and 42 dependent therefrom) is confusing in the recitation of "the fragment encodes a polynucleotide". A nucleic acid does not encode a polynucleotide. It appears the term should read "the fragment encodes a polypeptide" and the claim has been examined accordingly. It is suggested that applicants clarify the meaning of the claim.

8. Claims 31 (claims 38, 39, and 44 dependent therefrom) and 32-34 (claims 40, 41, and 45 dependent therefrom) are unclear in the recitation of "capable of identifying a polynucleotide encoding a polypeptide having alpha galactosidase activity". It is unclear from the claims and the specification as to the meaning of the term. While polynucleotides have the ability to hybridize to other polynucleotides, it is unclear as to how a polynucleotide is capable of identifying a polynucleotide encoding a polypeptide having alpha galactosidase activity. It is suggested that applicants clarify the meaning of the term.

Claim Rejections - 35 USC § 112, First Paragraph

9. In view of the amendment to claims 1 and 5 to remove part (c) from claims 1 and 5, the written description and scope of enablement rejections of claims 1-3, 5-9, and 17-23 under 35 U.S.C. 112, first paragraph, are withdrawn.

10. Claim 28 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is a new matter rejection. The examiner can find no support for the hybridization conditions of "wash in fresh 1X SET at –10 degrees Celsius". It is noted that the conditions are similar to those disclosed at page 6 of the specification. However, the conditions as recited in the claims are not supported by the claims, specification or drawings as originally filed.

11. Claims 24, 25, and 27-45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 24 is drawn to a genus of isolated polynucleotides that hybridize to a polynucleotide encoding SEQ ID NO:4, or a complement thereof, and wherein the isolated polynucleotide has alpha-galactosidase activity, and optionally wherein the polynucleotide encoding SEQ ID NO:4 is SEQ ID NO:1, 2, or 3, and optionally wherein the hybridization conditions are of low stringency as recited in claims 27 and 28. Claims 29 (claim 42 dependent therefrom), 30 (claim 43 dependent therefrom), 35, 36, and 37 are drawn to a genus of nucleic acid fragments comprising a portion or 15, 30, or 50 bases of a nucleic acid sequence of a polynucleotide of claims 1, 5, or 24 or a polynucleotide encoding SEQ ID NO:4 wherein the fragment encodes a polypeptide having alpha-galactosidase activity. Claims 31 (claim 44 dependent therefrom), 33 and 34 (claim 45 dependent therefrom), and 38-41, are drawn to a genus of nucleic acid fragments consisting of a portion or 30 or 50 bases of the polynucleotide of claims 1, 5, or 24, a polynucleotide encoding SEQ ID NO:4, or the polynucleotide of SEQ ID NO:1, 2, or 3 with the

capability of identifying a polynucleotide encoding a polypeptide having alpha galactosidase activity. Claims 32 (claim 45 dependent therefrom), 40, and 41 are drawn to a genus of nucleic acid fragments that hybridize to a polynucleotide encoding SEQ ID NO:4 or a complement thereof, and are capable of identifying a polynucleotide encoding a polypeptide having alpha galactosidase activity. The genus of claimed polynucleotides as described above have not been adequately described in the specification. The specification teaches the structure of only a single representative species of such polynucleotides, i.e., SEQ ID NO:3. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of hybridizing to a polynucleotide encoding SEQ ID NO:4, encoding a polypeptide having alpha galactosidase activity, and/or capable of identifying a polynucleotide encoding a polypeptide having alpha galactosidase activity. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Applicants argue new claims 24 and 29-45 are sufficiently described to meet the written description requirement of 35 USC 112, first paragraph. Applicants' argument is not found persuasive. As stated above, applicant has not met the written description requirement of 35 USC 112, first paragraph because the structure of the claimed genus of polynucleotides has not been described as detailed above.

12. Claims 24, 25, and 27-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polynucleotide of SEQ ID NO:3, does not reasonably provide enablement for: all polynucleotides that hybridize under any conditions to a polynucleotide encoding SEQ ID NO:4, or a complement thereof, and wherein the isolated polynucleotide has alpha-galactosidase activity (claim 24), and optionally wherein the polynucleotide encoding SEQ ID NO:4 is SEQ ID NO:1, 2, or 3 (claim 25), and optionally wherein the hybridization conditions are of low stringency as recited in claims 27 and 28; all nucleic acid fragments comprising a portion or 15, 30, or 50 bases of a nucleic acid sequence of a polynucleotide of claims 1, 5, or 24 or a polynucleotide encoding SEQ ID NO:4 wherein the fragment encodes a polypeptide having alpha-galactosidase activity (claims 29, 30, and 35-37); all

nucleic acid fragments consisting of a portion or 30 or 50 bases of the polynucleotide of claims 1, 5, or 24, a polynucleotide encoding SEQ ID NO:4, or the polynucleotide of SEQ ID NO:1, 2, or 3 with the capability of identifying a polynucleotide encoding a polypeptide having alpha galactosidase activity (claims 31, 33, 34, and 38-4); and all nucleic acid fragments that hybridize to a polynucleotide encoding SEQ ID NO:4 or a complement thereof, and are capable of identifying a polynucleotide encoding a polypeptide having alpha galactosidase activity (claims 32, 40, and 41). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re* Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 24, 25, 27, 28, 29 (claim 42 dependent therefrom), 30 (claim 43 dependent therefrom), 31 (claim 44 dependent therefrom), 33, 34 (claim 45 dependent therefrom), and 35-41 encompass all polynucleotides as describe above. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims.

While the specification is enabling for the polynucleotide of SEQ ID NO:3, the specification is not enabling for the entire scope of polynucleotides as broadly encompassed by the claims as undue experimentation would be required for a skilled artisan to make the entire scope of claimed polynucleotides. The specification provides guidance and a single working example for making *only* the polynucleotide of SEQ ID NO:3 using alpha galactosidase activity assays to screen for polynucleotides encoding polypeptides having alpha galactosidase activity (see pages 18-20 of the instant specification). The specification does not provide guidance or working examples for isolating all polynucleotides as

broadly encompassed by the claims. The disclosed isolation method as presented in the working examples is dependent solely on the activity of an encoded polypeptide and not structural homology. As such, one of skill in the art would recognize that this method *is not* applicable to making the entire scope of claimed polynucleotides from any source, particularly those polynucleotides comprising fragments or portions of a polynucleotide encoding SEQ ID NO:4 or fragments and portions of SEQ ID NOs:1-3. While other methods of nucleic acid isolation are known in the art, these methods, e.g., hybridization and/or PCR, are dependent upon sufficient structural homology for their successful application. Therefore, in order to isolate the claimed polynucleotides by hybridization or PCR using the disclosed sequences and portions and fragments thereof, one of skill in the art must determine the appropriate conditions for isolation of *all* claimed polynucleotides (which will vary depending on the fragment or variant used in the hybridization reaction). Furthermore, the specification does not provide guidance as to the presence of polynucleotides encoding polypeptides with alpha galactosidase activity in other organisms or regions of homology shared among nucleic acids encoding alpha galactosidase polypeptides. One of skill in the art would recognize that fragments and portions of a polynucleotide encoding SEQ ID NO:4 or the polynucleotide of SEQ ID NO3, or the polynucleotides of SEQ ID NOs:1 and 2, being fragments of SEQ ID NO:3 of 52 and 31 nucleotides, respectively, are highly unlikely to encode polypeptides having alpha galactosidase activity. There is no disclosure of the catalytic domain of SEQ ID NO:3 or the residues of the structure of SEQ ID NO:3 that are necessary for catalytic activity. There is no guidance in the specification that polynucleotide fragments of a polynucleotide encoding SEQ ID NO:4 or the polynucleotide of SEQ ID NO3, or the polynucleotides of SEQ ID NOs:1 and 2 encode polypeptides having alpha galactosidase activity. Therefore, it is highly unpredictable that if such fragments were found within a larger polypeptide that the larger polypeptide would exhibit alpha galactosidase activity. Furthermore, the specification provides no guidance or working examples to demonstrate that such fragments found within a larger polynucleotide would encode polypeptides exhibiting alpha galactosidase activity. Even if a skilled artisan were to use SEQ ID NO:1 or 2 to isolate other polynucleotides by, for example, hybridization assay or PCR, a high degree of unpredictability remains as to whether such polynucleotides

would encode polypeptides having alpha galactosidase activity. There exists a high degree of unpredictability as to whether all polynucleotides as encompassed by the claims could be isolated by methods that are solely dependent on enzyme activity or structural homology using the guidance provided in the instant specification without undue experimentation. One of skill in the art would be left to screen an *infinite number* of polynucleotides with a fragment or portion of a polynucleotide encoding SEQ ID NO:4 or the polynucleotides of SEQ ID NO:1, 2, or 3 in order to determine if such polynucleotides encode polypeptides with alpha galactosidase activity.

Therefore, it would constitute undue experimentation for a skilled artisan to make all polynucleotides as broadly encompassed by the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re* Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re* Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

The examiner has addressed applicant's arguments to the extent the arguments apply to the instant rejection. Applicants argue (beginning at page 11 of Paper No. 22) that it would not require undue experimentation to make all polynucleotides as encompassed by the claims. Applicants argue the amino acid sequence (SEQ ID NO:4) and the encoding nucleic acid sequence (SEQ ID NO:3) have been disclosed and along with standard laboratory techniques using these sequences, one of skill in the art could isolate and screen for polynucleotides encoding polypeptides having alpha galactosidase activity. Applicants argue that such routine screening would not constitute undue experimentation. Applicants' argument is not found persuasive. As stated above, insufficient guidance is provided for making all claimed polynucleotides with the predictability of such polynucleotides encoding polypeptides having alpha galactosidase activity without undue experimentation.

Conclusion

13. All claims are rejected. No claim is in condition for allowance.

Applicant's addition of new claims 24-45 necessitated the new ground(s) of rejection presented in this office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally be reached Monday-Friday from 7:30 am to 2:00 pm and from 3:30 pm to 5:30 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX number for this Group is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1652